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| EXAMINER |
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| BABIC, CHRISTOPHER M |

| ART UNIT | PAPER NUMBER |
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| 1637 | |

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DATE MAILED: 09/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/673,575 | SINHA ET AL. | |
| | Examiner | Art Unit | |
| | Christopher M. Babic | 1637 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *22 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-9,21 and 22* is/are pending in the application.

4a) Of the above claim(s) *10-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,21 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/30/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Election/Restrictions*

Applicant's election with traverse of Group I (Claims 1-9, 21, 22) in the reply filed on July 22, 2005 has been considered and deemed not persuasive. The traversal is on the ground(s) that there is no search burden on the Examiner. Applicants are correct in asserting that a *sequence search* of Claim 3 will include a *sequence search* of Claim 10. However, the textual based search of Claim 10 would encompass *any* polymerase chain reaction (PCR), as opposed to only *Alu* based PCR reactions as those in Claim 3. Furthermore, many oligonucleotide primers, as those presented in Claims 3 and 10, are not disclosed in nucleic acid databases and require a manual examination of suspected applicable references (i.e. primers).

The requirement is still deemed proper and is therefore made FINAL.

### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

**1. Claims 1-3 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Palmirotta et al. ("Origin and Gender Determination of Dried Blood on a Statue**

**of the Virgin Mary" Journal of Forensic Science. March 1998. (43) 2, Pages 431-434).**

Regarding Claim 1, Palmirotta et al. disclose a process for quantitating a human DNA in a sample, said process comprising the steps of: providing a sample to be analyzed (Page 432, Column 2, Paragraphs 2,3); amplifying predetermined genomic DNA containing an Alu element by using primers (Page 432, Column 2, Paragraph 3) said Alu element being enriched in the human genome (Figure 1, Lane1) compared to non-human primates genomes (Figure 1, Lanes 9-15); and quantitating the human DNA by comparing the amplified DNA with a reference (Figure 1).

Regarding Claim 2, Palmirotta et al. disclose inter-Alu PCR by referencing the protocol used by Tagle et al. (See included Tagle et al. reference) (Page 432, Column 2, Paragraph 3).

Regarding Claim 3, Palmirotta et al. disclose the *exact* primer sequences of SEQ ID NO:1 (5'- GATCGCGCCACTGCACTCC-3') and SEQ ID NO: 2 (5'-GGATTACAGGCGTGAGCCAC-3') (Page 432, Column 2, Paragraph 3).

Regarding Claim 7, Palmirotta et al. disclose detecting the human DNA on an agarose gel stained with ethidium bromide (Figure 1).

**2. Claims 1-2, 7, 21, and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Carroll et al. ("Large-scale Analysis of the Alu Ya5 and Yb8**

**Subfamilies and their Contribution to Human Genomic Diversity" Journal of Molecular Biology. 2001. 311, Pages 17-40).**

Regarding Claim 1, Carroll et al. disclose a process for quantitating a human DNA in a sample, said process comprising the steps of: providing a sample to be analyzed (Page 38, Column 1, Paragraphs 2); amplifying predetermined genomic DNA containing an Alu element by using primers (Page 38, Column 2, Paragraph 1) said Alu element being enriched in the human genome (Abstract) compared to non-human primates genomes (Abstract); and quantitating the human DNA by comparing the amplified DNA with a reference (Page 38, Column 2, Paragraph 1).

Regarding Claim 2, Carroll et al. disclose inter-Alu PCR (Page 38, Column 2, Paragraph 1).

Regarding Claim 7, Carroll et al. disclose detecting the human DNA on an agarose gel stained with ethidium bromide (Page 38, Column 2, Paragraph 1).

Regarding Claim 21, Carroll et al. disclose a process for quantitating a human DNA in a sample, said process comprising the steps of: providing a sample to be analyzed (Page 38, Column 1, Paragraphs 2); amplifying predetermined genomic DNA containing an Alu element by using primers (Page 38, Column 2, Paragraph 1), said Alu element being present only in the human genome (Abstract); and quantitating the human DNA by comparing the amplified DNA with a reference (Page 38, Column 2, Paragraph 1).

Regarding Claim 22, Carroll et al. disclose a process for quantitating a human DNA in a sample, said process comprising the steps of: providing a sample to be analyzed (Page 38, Column 1, Paragraphs 2); amplifying predetermined genomic DNA containing an young Alu element by using primers (Page 38, Column 2, Paragraph 1), said young Alu element being largely absent from non-human primates (Abstract); and quantitating the human DNA by comparing the amplified DNA with a reference (Page 38, Column 2, Paragraph 1).

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

**1. Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Palmirotta et al. ("Origin and Gender Determination of Dried Blood on a Statue of the Virgin Mary" Journal of Forensic Science. March 1998. (43) 2, Pages 431-434) or Carroll et al. ("Large-scale Analysis of the Alu Ya5 and Yb8 Subfamilies and their Contribution to Human Genomic Diversity" Journal of Molecular Biology. 2001. 311, Pages 17-40), in view of Hoglund et al. ("Isolation and characterization of radiation hybrids for human chromosome 12" Cytogenetic Cell Genetics. 1995. 69, Pages 240-245).**

Regarding Claim 4, the methods of Palmirotta et al. or Carroll et al. have been outlined in the above rejections. Neither Palmirotta et al. nor Carroll et al. specifically disclose the practice of an *intra*-ALU PCR.

Hoglund et al. disclose the practice of an intra-ALU PCR to identify somatic cell hybrids retaining human material (Abstract; Page 241, Column 1, Paragraph 5).

Based on the disclosure of Hoglund et al, one of ordinary skill in the art at the time of invention would have had a reasonable expectation of success performing an intra-ALU PCR in the methods of Palmirotta et al. or Carroll et al. The motivation to do so, provided by the disclosure of Hoglund et al., would have been to identify DNA that contained human specific material (Abstract; Page 244, Column 1, Paragraph 1). It would have been *prima facie* obvious to one of ordinary skill in the art at the time of invention to practice the methods as claimed.

**2. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Carroll et al. ("Large-scale Analysis of the Alu Ya5 and Yb8 Subfamilies and their Contribution to Human Genomic Diversity" Journal of Molecular Biology. 2001. 311, Pages 17-40) in view of Hoglund et al. ("Isolation and characterization of radiation hybrids for human chromosome 12" Cytogenetic Cell Genetics. 1995. 69, Pages 240-245), in further view of Jurka ("A new subfamily of recently retroposed human Alu repeats" Nucleic Acids Research. 1993. Vol. 21. No. 9, Page 2252).**

Regarding Claim 5, the methods of Carroll et al. and Hoglund et al. have been outlined in the above rejections. Carroll et al. do not specifically disclose the *exact* primer sequences of SEQ ID NO: 3 and SEQ ID NO: 4, drawn to the Yb8 Alu subfamily.

Jurka discloses the entire Sb2 Alu subfamily sequence (Figure 1). The term "Sb2" is considered to older nomenclature of the Yb8 subfamily (See reference: Batzer et al. "Standardized Nomenclature for Alu Repeats" Journal of Molecular Evolution. 1996. 42, Pages 3-6).

The *identical* primer sequence presented in SEQ ID NO: 3 (5'-CGAGGCGGGTGGATCATGAGGT-3' is contained in the sequence provided by Jurka (Figure 1) from nucleotides 48-69. Furthermore, the *identical* complement of the primer sequence (i.e. reverse primer) presented in SEQ ID NO: 3 (5'-

TCTGTCGCCCAGGCCGGACT -3' is contained in the sequence provided by Jurka (Figure 1) from nucleotides 273-254.

Based on the disclosure of Jurka, one of ordinary skill in the art would have had a reasonable expectation of success using the primers presented in SEQ ID NO: 3 and SEQ ID NO: 4 to amplify a portion of the Yb8 Alu subfamily in the methods of Carroll et al. The motivation to so would have been 100% local similarity of the instant primers in the sequence provided by Jurka. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of invention to practice the methods as claimed.

**3. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Carroll et al. ("Large-scale Analysis of the Alu Ya5 and Yb8 Subfamilies and their Contribution to Human Genomic Diversity" Journal of Molecular Biology. 2001. 311, Pages 17-40) in view of Hoglund et al. ("Isolation and characterization of radiation hybrids for human chromosome 12" Cytogenetic Cell Genetics. 1995. 69, Pages 240-245), in further view of Batzer et al. ("Standardized Nomenclature for Alu Repeats" Journal of Molecular Evolution. 1996. 42, Pages 3-6).**

Regarding Claim 6, the methods of Carroll et al. Hoglund et al. outlined in the previous rejections. Carroll et al. do not specifically disclose the *exact* primer sequences of SEQ ID NO: 5 and SEQ ID NO: 6, drawn to the Yd6 Alu subfamily.

Batzer et al. disclose that the younger subfamilies of Alu sequences contain individual members that are restricted to the human genome (Page 3, Column 2,

Paragraph 1). In addition, they disclose that the "Y" subfamily is considered a "gold standard" since it has been previously identified as a subfamily by a number of different laboratories (Page 4, Column 2, Paragraph 2). Moreover, they disclose that *all* Alu repeats presently known to retropose differ from the Y subfamily consensus sequence by only a *few* additional diagnostic mutations, suggesting that the younger subfamilies of Alu repeats were ancestrally derived from the Y subfamily; therefore, young subfamilies are defined as lineages that descended from this gold standard (Page 4, Column 2, Paragraph 2; Page 5, Column 1, Paragraph 1).

Based on the disclosure of Batzer et al., one of ordinary of skill in the art at the time of invention would have had a reasonable expectation of success using the primers presented in SEQ ID NO: 5 and SEQID NO: 6 to amplify the Yd6 subfamily for use in the methods of Carroll et al. Hoglund et al. The motivation to do so, provided by Batzer et al., would have been not only that the Yd6 subfamily would have been expected to be enriched in the human genome, but that the Yd6 subfamily would behave in a similar fashion than the Yb8 subfamily due to the fact lineages were derived from a common ancestor and only differ by a few diagnostic mutations. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of invention to practice the methods as claimed.

**4. Claims 7 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Palmirotta et al. ("Origin and Gender Determination of Dried Blood on a Statue of the Virgin Mary" Journal of Forensic Science. March 1998. (43) 2, Pages**

**431-434) or Carroll et al. ("Large-scale Analysis of the Alu Ya5 and Yb8 Subfamilies and their Contribution to Human Genomic Diversity" Journal of Molecular Biology. 2001. 311, Pages 17-40), in view of Gelmini et al. ("Quantitative polymerase chain reaction-based homogeneous assay with fluorogenic probes to measure c-*erb*B-2 oncogene amplification" Clinical Chemistry. 1997. 43:5, Pages 752-758).**

Regarding Claims 7 and 8, the methods of Palmirotta et al. or Carroll et al. have been outlined in the above rejections. Neither Palmirotta et al. nor Carroll et al. specifically disclose the practice of a quantitative PCR system such as *Taq*Man.

Gelmini et al. disclose the practice of a quantitative PCR system using *Taq*Man chemistry (Figures 1,2,3; Table 1; Page 754, Columns 1,2). Furthermore, they highlight the advantages of using fluorogenic probes in PCR, such as the circumventing of post-PCR product quantitation procedures (Page 752, Column 2, Paragraph 2).

Based on the disclosure of Gelmini et al., one of ordinary one of ordinary skill in the art at the time of invention would have had a reasonable expectation of success performing a quantitative PCR system using *Taq*Man chemistry. The motivation to do so, provided by Gelmini et al., would have been to circumvent the need for post-PCR product quantitation procedures. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of invention to practice the methods as claimed.

***Conclusion***

**No claims are allowed. No claims are free of the prior art.**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher M. Babic whose telephone number is 571-272-8507. The examiner can normally be reached on Monday-Friday 7:00AM to 4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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AU 1637

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

9/1/05